

10712258 09/20/05

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NEWS 8 SEP 22 MATHDI to be removed from STN

NEWS EXPRESS JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

| | |
|------------|---|
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10712258 09/20/05

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 30 SEP 2005 HIGHEST RN 864353-93-5
DICTIONARY FILE UPDATES: 30 SEP 2005 HIGHEST RN 864353-93-5

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TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

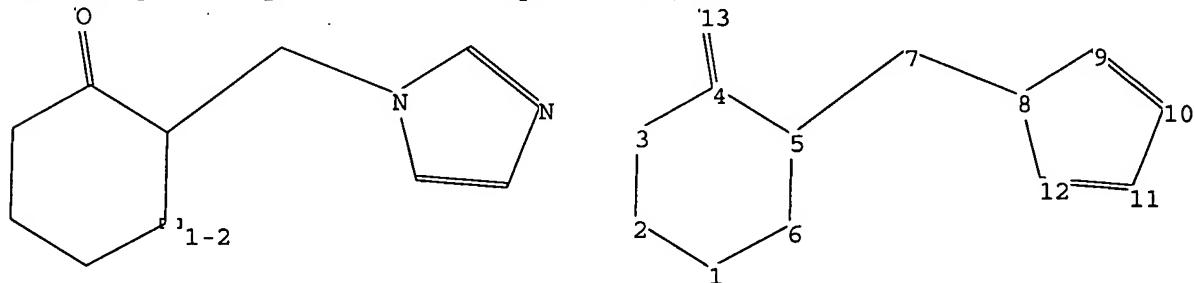
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>
Uploading C:\Program Files\Stnexp\Queries\10712258.str



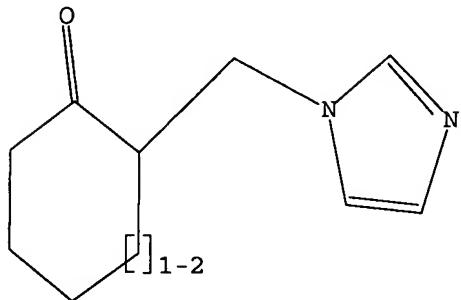
chain nodes :
7 13
ring nodes :
1 2 3 4 5 6 8 9 10 11 12
chain bonds :
4-13 5-7 7-8
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 8-9 8-12 9-10 10-11 11-12
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 4-13 5-6 7-8 8-9 8-12 9-10 10-11
exact bonds :
5-7 11-12
isolated ring systems :
containing 8 :

10712258 09/20/05

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 11
SAMPLE SEARCH INITIATED 15:13:09 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 496 TO ITERATE

100.0% PROCESSED 496 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 8584 TO 11256
PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

=> s 11 full
FULL SEARCH INITIATED 15:13:17 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 9119 TO ITERATE

100.0% PROCESSED 9119 ITERATIONS 24 ANSWERS
SEARCH TIME: 00.00.01

L3 24 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE TOTAL
FULL ESTIMATED COST ENTRY SESSION
161.33 161.54

FILE 'CAPLUS' ENTERED AT 15:13:25 ON 01 OCT 2005

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FILE COVERS 1907 - 1 Oct 2005 VOL 143 ISS 15
FILE LAST UPDATED: 30 Sep 2005 (20050930/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s 13
L4      22 L3

=> s 14 and oxazolidine
      3939 OXAZOLIDINE
      1268 OXAZOLIDINES
      4294 OXAZOLIDINE
          (OXAZOLIDINE OR OXAZOLIDINES)
L5      2 L4 AND OXAZOLIDINE

=> d ibib abs hitstr tot
```

L5 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:652673 CAPLUS

DOCUMENT NUMBER: 141:174173

TITLE: Process for the preparation of imidazolyl compounds
INVENTOR(S): Verbeek, Jan-Maarten; Van der Meij, Paulus F. C.

PATENT ASSIGNEE(S): Solvay Pharmaceuticals B.V., Neth.

SOURCE: U.S. Pat. Appl. Publ., 8 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

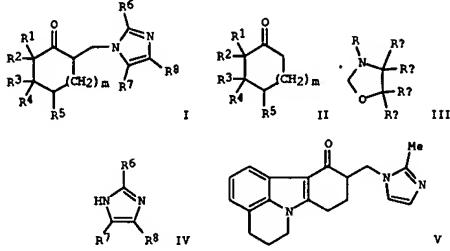
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--------|------------|-----------------|------------|
| US 2004158077 | A1 | 20040812 | US 2002-712258 | 20031114 |
| PRIORITY APPLN. INFO.: | | | EP 2002-79838 | A 20021118 |
| OTHER SOURCE(S): | MARPAT | 141:174173 | NL 2002-1021939 | A 20021118 |

GI

current application

G1



AB The invention discloses a method for the preparation of imidazolyl compds., such as I [R1, R3 = alkyl, alkoxyalkyl, optionally substituted aryl or heteroaryl; R1R3 = fused homocyclic or heterocyclic system comprising one or more rings; R2, R4 = H, double bond (optionally part of an aromatic system); R3 = H, alkyl, alkoxy, alkoxyalkyl, halogen; R4, R5, R6, R7, R8 = H, alkyl; m = 1 - 2; R6 = H, alkyl, acid addition salts], by reacting a cyclic ketone of formula II with an oxazolidine derivative III (R = H, alkyl optionally substituted with OH or an optionally substituted aryl group; Ra, Rb, Rc, Rd = H, alkyl), followed by reaction with an imidazole IV. Thus, 5,6,9,10-tetrahydro-4H-pyrido[3,2,1-k]carbazol-11(8H)-4-one and MeSO3H in BuOH were heated to 70° C and then treated with 3-oxazolidinethanol in BuOH, and the mixture was heated for 50 min at 80° C. Then, 2-methylimidazole in BuOH was added and the mixture was

L5 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:453190 CAPLUS

DOCUMENT NUMBER: 141:23529

TITLE: Novel process for the preparation of imidazolyl compounds, particularly ondansetron, cilanstren, and analogs, using oxazolidine derivatives as formaldehyde equivalents in a Mannich-like reaction

INVENTOR(S): Verbeek, Jan-Maarten; Van Der Meij, Paulus F. C.

PATENT ASSIGNEE(S): Solvay Pharmaceuticals B.V., Neth.

SOURCE: PCT Int. Appl., 22 pp.

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 200406116 | A1 | 20040603 | WO 2003-EP50841 | 20031117 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HP, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GE, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2504614 | AA | 20040603 | CA 2003-2504614 | 20031117 |
| EP 1565445 | A1 | 20050824 | EP 2003-811396 | 20031117 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |

PRIORITY APPLN. INFO.: EP 2002-79838 A 20021118

OTHER SOURCE(S): CASREACT 141:23529; MARPAT 141:23529

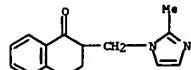
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to an improved method for the preparation of imidazolyl

compds. I [wherein: Ra, Rb = C1-C6 alkyl, C1-C6 alkoxyalkyl, optionally substituted aryl or heteroaryl; or RaRb = fused homocyclic or heterocyclic system comprising one or more rings; Ra'Rb' = H2, carbon-carbon double bond (optionally part of an aromatic system); Rc = H, C1-C6 alkyl, C1-C6 alkoxy, C1-C6 alkoxyalkyl, or halogen; Rd = H or C1-C4 alkyl; Re = H or C1-C4 alkyl; m = 1 or 2; R1 = H or C1-C4 alkyl; as well as acid addition salts]. The method is characterized in that a cyclic ketone of formula II reacts with an oxazolidine derivative III, followed by reaction with an imidazole IV, optionally followed by reaction with a suitable acid [wherein: R1, Rd, and Re = as given above; R = H, C1-C4 alkyl optionally substituted with OH or an optionally substituted aryl group; R', R'', R''', and R'''' = H or C1-C4 alkyl]. The method is especially useful for the preparation of selective neuronal 5-HT receptor antagonists, which are useful

useful

L5 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
stirred for 2 h at 120° C to afford V.HCl in 77% yield. The method is esp. useful for the prepn. of selective neuronal 5-HT receptor antagonists, which are useful as anti-migraine and antipsychotic agents.IT 697807-10-6 CAPLUS
RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)RN 697807-10-6 CAPLUS
CN 1-(2H)-Naphthalenone, 3,4-dihydro-2-[(2-methyl-1H-imidazol-1-yl)methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

L5 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN (Continued)
as anti-migraine and antipsychotic agents, e.g., ondansetron and cilanstren. The method is superior to prior art Mannich processes using formaldehyde, which give tar-like byproducts when scaled up. For instance, 1,2,3,9-tetrahydro-9-methyl-4H-carbazol-4-one and MeSO3H in BuOH were heated to 90° and then treated with 3-oxazolidinethanol in BuOH, and the mixt. was heated for 50 min at 80°. Then, 2-methylimidazole in BuOH was added and the mixt. was stirred for 2 h at 120°. Extn. and crystn. gave V.HCl, i.e. ondansetron HCl, in 70.1% yield and > 95% purity, with an addnl. 14.5% product in the mother liquor. Similar preps. of (+)-cilanstren HCl and another compd. are also given.

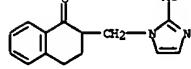
IT 697807-10-6, 3,4-Dihydro-2-[(2-methyl-1H-imidazol-1-yl)methyl]-1-(2H)-naphthalenone hydrochloride

RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(target compound; improved preparation of imidazole 5-HT antagonists (ondansetron and cilanstren) using oxazolidine derivs. as formaldehyde equivalent in Mannich-like reaction)

RN 697807-10-6 CAPLUS

CN 1-(2H)-naphthalenone, 3,4-dihydro-2-[(2-methyl-1H-imidazol-1-yl)methyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

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| | | |
|---------------------|-------|--------|
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| | | |
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| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE
ENTRY | TOTAL
SESSION |
|--|---------------------|------------------|

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